Remarks

Claims 1-20 and 43-61 were pending in the subject application. By this Amendment, claims 4-20 and 43-61 have been amended, claims 1-3, 21-42 and 62-69, have been canceled, and new claims 70-86 have been added. The undersigned avers that no new matter is introduced by this amendment. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 4-20, 43-61, and 70-86 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

The applicants have submitted with this Amendment formal Figures 1A-1C, 2A-2E, 3A-3C, 4A-4C, and 5 in response to the Notice of Draftsperson's Patent Drawing Review, pursuant to 37 C.F.R. §1.85(a). Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Claims 1-20 and 43-61 have been rejected under 35 U.S.C. §112, first paragraph, as non-enabled by the subject specification. The applicants respectfully submit that the claimed invention is fully enabled by the subject specification.

The claimed invention is directed to neural cells obtainable from umbilical cord blood, a method of producing such cells from umbilical cord blood, compositions comprising umbilical cord blood or a mononuclear cell fraction, and methods of making such compositions. The Office Action cites Jackowski *et al.* (1995) to support the assertion that the subject specification does not adequately teach how to use the recited cells for transplantation resulting in a therapeutic effect. Jackowski *et al.* indicates that certain endogenous molecules exist that inhibit regeneration of axons in the mammalian central nervous system and peripheral nervous system. However, the applicants note that the next paragraph, at page 311 of Jackowski *et al.* (column 2), indicates that initial growth cones of transplanted fetal neurons "are exempt from such inhibitory influences (emphasis added)." Furthermore, Jackowski *et al.* indicates that "the most exciting and potentially far-reaching therapeutic approach would modify the regenerative growth cones of disconnected but surviving adult central neurons so that they behave more like the growth cones of foetal neurons *ab initio*, *i.e.*, so that they are no longer susceptible to the neurite –growth inhibitory milieu of the adult mammalian CNS" (see paragraph bridging pages 311 and 312). As indicated at page 45, lines 30-33,

and page 46, line 1, of the specification, the cells of the claimed invention provide a stable, readily available source of neural stem cells, which become functional neurons and are capable of producing behavioral recovery at a comparable level to that observed with transplantation of fetal neurons. The accuracy of this statement is confirmed both by the examples within the subject specification and in the scientific literature, as discussed in detail below.

At page 3, the Office Action indicates that while general guidance is provided at pages 1-8 of the specification, there are no working examples described in the specification demonstrating a therapeutic effect upon transplantation of the claimed compositions. However, working examples demonstrating transplantation of human umbilical cord blood cells of the claimed invention are described at pages 58-72 of the subject specification.

The Office Action also indicates that the subject specification does not provide any guidance relating to the number of cells to inject, the site of injection, and the extent of cellular persistence required and attainable in practice, in order to confer a therapeutic benefit. The applicants respectfully disagree. Pages 58-65 of the subject specification describe working examples demonstrating the parenteral administration of human cord blood fractions in the treatment of neurological damage from ischemia (stroke). For example, page 58, lines 19-25, and page 60, lines 7-10, describe protocols followed for preparation of donor cells and subsequent implantation, including cell number. As described at pages 61-65 of the specification, histological and immunohistochemical assessment indicated that the human umbilical cord blood cells survived in the brain for several days post transplantation. Results of behavioral tests (*e.g.*, rotarod test, adhesive-removal somatosensory test, and modified neurological severity score), which are described at pages 60-61, 63-66, and Figures 3A-C, 4A-C, and 5, demonstrate significant improvement in functional outcome on motor, sensory, and modified NSS tests.

Furthermore, pages 66-72 of the subject specification describe experiments demonstrating that parenteral administration of human umbilical cord blood reduces neurological deficits after traumatic brain injury (TBI). At page 66, lines 8-15, the subject specification describes protocols followed for preparation of donor cells and subsequent implantation, including cell number. As described at page 68, lines 17-33. page 69, lines 1-27, and page 70, lines 1-31, histological assessment and three-dimensional image assessment showed that the transplanted human umbilical

cord blood cells survived several days post-transplantation. Results of behavioral tests, which are described at pages 68-72, demonstrate that the transplanted human umbilical cord blood cells reduced the motor neurological functional deficits caused by TBI.

In addition to the working examples described at pages 58-65 of the specification, submitted herewith is Zigova *et al.* (*Cell Transplantation*, 11:265-274, 2002), which supports the enablement of the claimed neural cells, compositions, and methods of producing neural cells for cell therapy. Zigova *et al.* describes the transplantation of human umbilical cord blood (HUBC) cells into the brains of developing rats. Results of the experiment showed that approximately 20% of transplanted HUCB survived in the absence of immunosuppression within the neonatal brain. Additionally, immunocytochemistry showed that at least some of the transplanted HUCB cells differentiated into cells with distinct glial or neuronal phenotypes in response to instructive signals within the host's brain.

The asserted unpredictability in the art is only discussed within the Office Action in the context of methods of treatment using neural cells, *e.g.*, administration of neural cells of the subject invention. The applicants note that while cancelled claims 21-42 and 62-69 are directed to methods of treatment, the rejected claims are directed neural cells, compositions comprising neural cells, methods of producing neural cells from umbilical cord blood, methods of producing enriched neural cells, and methods for producing pharmaceutical compositions comprising neural cells. When rejecting a claim under the enablement requirement of 35 U.S.C. §112, the Patent Office bears an initial burden of setting forth a reasonable explanation as to why it believes the scope of protection provided by the claim is not adequately enabled by the specification of the application; this includes providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The applicants respectfully submit that the Patent Office has not met this burden. The only reasons set forth by the Office Action in support of the enablement rejection are based on purported unpredictability in neural cell therapy (based on Jackowski *et al.*), and the assertion that there is a lack of "working examples" in the specification. Both of these issues have been addressed above.

The applicants note that no rejection under 35 U.S.C. §101, for lack of utility, has been set forth in conjunction with the rejection under 35 U.S.C. §112, first paragraph. Nonetheless, if the

Examiner is suggesting that the cells of the claimed invention lack utility, outside of transplantation therapy, the applicants respectfully traverse and submit that there are other specific and credible utilities for the claimed cells. For example, the cells of the claimed invention can be proliferated in great numbers and induced to differentiate along various neural lineages. The proteins produced at various stages of cell development can be harvested. Alternatively, as indicated at page 20, lines 26-34, page 23, lines 18-27, and page 45, line 19, of the specification, the claimed cells can be transduced with a polynucleotide encoding a polypeptide of interest, permitting recombinant production of the polypeptide. For example, transfection of cord blood cells with an adenoviral vector bearing a green fluorescent protein (GFP) gene under the control of the Mushashi-1 promoter resulted in expression of GFP, as described at page 46, lines 16-32, and page 47, lines 1-6, of the specification. Therefore, the applicants respectfully submit that the cells of the claimed invention have a specific and credible utility and are fully enabled by the subject specification.

In view of the above remarks and amendments to the claims, the applicants respectfully submit that the pending claims are fully enabled by the specification as filed and, therefore, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Claims 2, 4-7, 8-14, 17-20, and 43-61 have been rejected under 35 U.S.C. §112, second paragraph, as indefinite. The applicants have addressed each aspect of the rejection in the paragraphs that follow.

The Office Action indicates that the term "silencers" recited in claims 2, 5, 7, 8-10, 13, 14, and 19 is unclear. The applicants respectfully submit that, given the benefit of the subject specification (*e.g.*, page 18, lines 28-32, and page 19, lines 1-15), one of ordinary skill in the art would understand the term to mean a differentiation agent, such as glial-cell missing silencer factor or neuron-restrictive silencer factor, that is capable of reducing or eliminating the expression of a gene. Submitted herewith for the Examiner's consideration is an excerpt from the *Glossary of Biotechnology and Genetic Engineering* (Zaid, A. *et al.*, Food and Agriculture Organization of the United States (F.A.O.), Research and Technology Publication No. 7, December, 1999), which provides a definition of the term "silencer" as it is commonly used in the art.

The Office Action indicates the phrase "cell signaling molecules" recited in claims 2, 5, 7, 8-10, 13, 14, and 19 is unclear. The applicants respectfully submit that the claims are not indefinite. However, by this Amendment, the applicants have deleted this phrase from the claims.

The Office Action indicates the term "neuroproteins" recited in claims 2, 5, 7, 8-10, 13, 14, and 19 is unclear. The applicants respectfully submit that the claims are not indefinite. However, by this Amendment, the applicants have deleted the term "neuroproteins" from the claims.

The Office Action indicates that the phrase "said stem or progenitor cells" in claim 4 lacks antecedent basis. By this Amendment, the applicants have amended step (a) in claim 4 to recite "wherein said mononuclear cells comprise stem or progenitor cells", providing antecedent basis for the phrase in step (b).

The Office Action indicates that recitation of the phrase "pluripotent stem or progenitor cells within said mononuclear cells" renders claims 11-14 and 17-19 indefinite. By this Amendment, the applicants have amended claim 11 to replace the phrase "pluripotent stem or progenitor cells within said mononuclear cells" with the phrase "said pluripotent or progenitor cells within said sample of mononuclear cells", which lends greater clarity to the claimed subject matter.

The applicants have amended claims 7 and 14 to recite that the differentiation agent comprises fetal or mature neuronal cells selected from the group consisting of mesencephalic cells and striatal cells.

The applicants have amended claims 17 and 18 to depend from claim 15, which provides the required antecedent basis for the terms "anti-proliferative agent" and "mitogen".

The applicants have amended claim 20 to depend from claim 19, which provides the required antecedent basis for the term "retinoic acid".

The applicants have amended claim 43 to recite that the amount of neural differentiation agent within the composition is effective to induce a neural phenotype in the pluripotent stem or progenitor cells within the umbilical cord blood or mononuclear fraction. Support for this amendment can be found, for example, at page 14, lines 7-19, of the specification, and the claims as originally filed.

The applicants have amended claims 44-49, which are method claims, to depend from method claim 43, instead of claim 40, which is a composition claim.

The applicants have amended claim 50 to replace the phrase "said umbilical cord blood" with "umbilical cord blood".

The applicants have amended claim 53 to depend from claim 51, which provides the required antecedent basis for the phrase "said neuronal cells".

The applicants have amended claim 54 to recite that the cells obtained from step (c) are combined with a pharmaceutically acceptable carrier, additive, or excipient.

The applicants have amended claim 57 to recite that, in step (b), the mononuclear cells are grown for a period sufficient to change the phenotype of the pluripotent stem or progenitor cells within the sample of mononuclear cells to neural. Additionally, the applicants have amended step (c) to recite that the cells having a neural phenotype are isolated from the pluripotent stem or progenitor cells within the sample of mononuclear cells. The applicants have also amended step (d) to replace the term "neural cells" with "cells having a neural phenotype".

By this Amendment, the applicants have added claims 70-71. Support for claims 70-71 can be found, for example, at page 9, lines 22-33, page 10, lines 1-5, page 18, lines 28-32, page 19, lines 1-5, as well as the claims as originally filed.

In view of the above remarks and the amendments to the claims, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Claims 1-3 have been rejected under 35 U.S.C. §102(b) as being anticipated by Kopen *et al.* (*Proc. Natl. Acad. Sci. USA*, 1999, 96:10711-10716). In addition, claims 1-3 have been rejected under 35 U.S.C. §102(b) as being anticipated by Reynolds *et al.* (*Science*, 1992, 255:1707-1710). The applicants respectfully submit that the claimed invention is not described or suggested by the cited references. However, by this Amendment, the applicants have cancelled claims 1-3, rendering this rejection moot.

The applicants note that the prior art rejection of claims 1-3 based on the Kopen *et al.* publication cites 35 U.S.C. §102(b) for statutory support. However, the publication date of the Kopen *et al.* publication appears to be September, 1999, which is less than one year prior to the subject application's earliest claimed priority date, *i.e.*, March 9, 2000. Therefore, the applicants respectfully submit that the Kopen *et al.* publication is not available as a prior art reference under 35 U.S.C. §102(b).

By this Amendment, the applicants have also added claims 72-86. Support for claims 72-74 can be found, for example, at pages 40-43, including Tables 1 and 2, of the subject specification. Support for claims 75-76 can be found, for example, at page 17, lines 1-3 of the specification. Support for claims 77-79 can be found, for example, at page 18, lines 28-32, page 19, lines 1-15, and page 30, lines 1-16, of the specification. Support for claim 80 can be found, for example, at page 20, lines 26-33, and page 23, lines 20-27, of the specification. Support for claim 81 can be found, for example, at pages 40-43 of the specification. Support for claims 82-86 can be found throughout the subject specification and claims as originally filed.

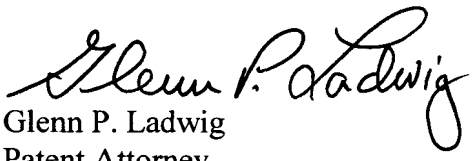
Claim 72 recites an isolated neural cell obtainable from umbilical cord blood, wherein the neural cell exhibits an increase in expression of genes associated with neurogenesis and a decrease in expression of genes associated with hematopoiesis when the cells are in the presence of an effective amount of a differentiation agent. Claim 81 further recites that the cell is a human multipotent neural progenitor cell. In contrast, the Kopen *et al.* and Reynolds *et al.* publications describe murine marrow stromal cells (MSCs) and murine neuroepithelial stem cells, respectively. In order to anticipate under 35 U.S.C. §102(b), a single reference must disclose within the four corners of the document each and every element and limitation contained in the rejected claim. *Scripps Clinic & Research Foundation v. Genentech*, 18 USPQ 2d 1001, 1010 (Fed. Cir. 1991). The cited references do not describe cells characterized by the expression pattern recited in claims 72-81, human or otherwise. Thus, the applicants respectfully submit that the cited references do not teach or suggest every element of the applicants' claimed invention. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b) is respectfully requested.

In view of the foregoing remarks and amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachments: Petition and Fee for Two-Month Extension of Time
Marked-Up Version of Amended Claims
Formal Drawings
Zigova *et al.* publication
Excerpt from Glossary of Biotechnology and Genetic Engineering

**Marked-Up Version of Amended Claims**

Claim 4 (Amended):

A method of producing neural cells from umbilical cord blood comprising:

[a.] (a) obtaining a sample of mononuclear cells from said umbilical cord blood, wherein said mononuclear cells comprise pluripotent stem or progenitor cells; and

[b.] (b) growing said mononuclear cells from step (a) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said stem or progenitor cells to neural.

Claim 5 (Amended):

The method according to claim 4, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erthyopoietin, thrombopoietin, silencers, SHC, [neuroproteins,] proteoglycans, glycoproteins, neural adhesion molecules, [cell signalling molecules and mixtures, thereof] and mixtures thereof.

Claim 6 (Amended):

The method according to claim 4, wherein said differentiation agent is a mixture of retinoic acid and NGF.

Claim 7 (Amended):

The method according to claim 5, wherein said [neuronal cells are] differentiation agent comprises fetal or mature neuronal cells selected from the group consisting of mesencephalic cells and striatal cells.

Claim 8 (Amended):

A method of producing neural cells from umbilical cord blood comprising:

[a.] (a) obtaining a sample of mononuclear cells from said umbilical cord blood, wherein said mononuclear cells comprise pluripotent stem or progenitor cells;

[b.] (b) selecting for and isolating [a sample of] said pluripotent stem or progenitor cells within said sample of mononuclear cells; and

[c.] (c) growing said stem or progenitor cells from step (b) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said stem or progenitor cells to neural.

Claim 9 (Amended):

The method according to claim 8, wherein said selecting and isolating step b is carried out using a magnetic cell separator to separate out cells containing a CD marker.

Claim 10 (Amended):

The method according to claim 8, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erthyopoietin, thrombopoietin, silencers, SHC, [neuroproteins,] proteoglycans, glycoproteins, neural adhesion molecules, [cell signalling molecules and mixtures, thereof] and mixtures thereof.

Claim 11 (Amended):

A method of producing neural cells from umbilical cord blood comprising:

[a.] (a) obtaining a sample of mononuclear cells from said umbilical cord blood, wherein said mononuclear cells comprise pluripotent stem or progenitor cells;

[b.] (b) growing said mononuclear cells from step [b] (a) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said pluripotent stem or progenitor cells within said sample of mononuclear cells to neural; and

[c.] (c) selecting for and isolating said neural cells from said [sample of] pluripotent stem or progenitor cells within said sample of mononuclear cells by essentially eliminating from said sample mononuclear cells having a CD marker.

Claim 12 (Amended):

The method according to claim 11, wherein said selecting and isolating step (c) is carried out using a magnetic cell separator to separate out cells containing a CD marker.

Claim 13 (Amended):

The method according to claim 11, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erthyopoietin, thrombopoietin, silencers, SHC, [neuroproteins,] proteoglycans, glycoproteins, neural adhesion molecules, [cell signalling molecules and mixtures, thereof] and mixtures thereof.

Claim 14 (Amended):

The method according to claim 13, wherein said [neuronal cells are] differentiation agent comprises fetal or mature neuronal cells selected from the group consisting of mesencephalic cells and striatal cells.

Claim 15 (Amended):

A method of producing a sample of enriched neural cells from a sample of mononuclear cells obtained from umbilical cord blood comprising:

[a.] (a) subjecting the mononuclear cells to an amount of an [anti-proliferating cell agent] anti-proliferative agent effective to eliminate essentially all proliferating cells from said mononuclear cell sample;

[b.] (b) exposing the remaining non-proliferating cells from step (a) to a mitogen to provide a population of differentiated cells and quiescent cells comprising a population of pluripotent stem or progenitor cells;

[c.] (c) growing said population of said differentiated cells and quiescent cells from step (b) to selectively grow said quiescent cells to the essential exclusion of said differentiated cells.

Claim 16 (Amended):

The method according to claim 15, comprising the further step of incubating a cell population obtained from step (c) to a differentiation agent effective to induce a neural phenotype in said pluripotent stem or progenitor cells.

Claim 17 (Amended):

The method according to [claim 11] claim 15, wherein said [anti-proliferative cell agent] anti-proliferative agent is Ara-C.

Claim 18 (Amended):

The method according to [claim 11] claim 15, wherein said mitogen is selected from the group consisting of epidermal growth factor and pokeweed mitogen.

Claim 19 (Amended):

The method according to [claim 12] claim 16, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erthyopoietin, thrombopoietin, silencers, SHC, [neuroproteins,] proteoglycans, glycoproteins, neural adhesion molecules, [cell signalling molecules and mixtures, thereof] and mixtures thereof.

Claim 20 (Amended):

The method according to [claim 15 wherein said retinoic acid is selected from 9-cis retinoic acid, all transretinoic acid and mixtures, thereof] claim 19, wherein said differentiation agent is a retinoic acid selected from the group consisting of 9-cis retinoic acid, all transretinoic acid, and a mixture thereof.

Claim 43 (Amended):

A composition comprising umbilical cord blood or a mononuclear cell fraction, thereof, in combination with an effective amount of at least one neural differentiation agent, wherein said

umbilical cord blood or mononuclear cell fraction comprise pluripotent stem or progenitor cells, and wherein said amount of neural differentiation agent is effective to induce a neural phenotype in said pluripotent stem or progenitor cells .

Claim 44 (Amended):

The composition according to claim 40, further comprising a cell medium to which said differentiation agent is added.

Claim 45 (Amended):

The composition according to claim 40, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature mesencephalic or striatal cells, brain derived neurotrophic factor (BDNF), glial derived neurotrophic factor (GDNF), glial growth factor (GFF), nerve growth factor (NGF), fibroblast growth factor (FGF), transforming growth factors (TGF), ciliary neurotrophic factor (CNTF), bone-morphogenetic proteins (BMP), leukemia [inhbitory] inhibitory factor (LIF), glial growth factor (GGF), tumor necrosis factors (TNF), interferon, insulin-like growth factors (IGF), colony stimulating factors (CSF), KIT receptor stem cell factor (KIT-SCF), interferon, triiodothyronine, thyroxine, erythropoietin, thrombopoietin, glial-cell missing silencer factor, neuron restrictive silencer factor, SRC-homology-2-domain-containing transforming protein, [neuroproteins,] proteoglycans, glycoproteins, [and] neural adhesion molecules, and mixtures thereof.

Claim 46 (Amended):

The composition according to claim 40, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature mesencephalic or striatal cells, brain derived neurotrophic factor (BDNF), glial derived neurotrophic factor (GDNF), glial growth factor (GFF), [nerve growth factor (NGF) and mixtures, thereof] nerve growth factor (NGF), and mixtures thereof.

Claim 47 (Amended):

The composition according to claim 40, wherein said differentiation agent is selected from the group consisting of mixtures of retinoic acid, brain derived neurotrophic factor (BDNF), glial derived neurotrophic factor (GDNF), glial growth factor (GFF), and nerve growth factor (NGF).

Claim 48 (Amended):

The composition according to claim 44, further comprising a cell medium to which said differentiation agent is added.

Claim 49 (Amended):

The composition according to claim 40, wherein said differentiation agent is a mixture of retinoic acid and nerve growth factor.

Claim 50 (Amended):

A method of producing a pharmaceutical composition comprising a sample of mononuclear cells being enriched with cells having a neural phenotype marker, said method comprising:

[a.] (a) obtaining a sample of mononuclear cells from [said] umbilical cord blood, wherein said mononuclear cells comprise stem or progenitor cells; and

[b.] (b) growing said mononuclear cells from step (a) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said stem or progenitor cells to neural; and

[c.] (c) combining said cells obtained from step (b) with a pharmaceutically acceptable carrier, additive or excipient.

Claim 51 (Amended):

The method according to claim 50, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erthyopoietin,

thrombopoietin, silencers, SHC, [neuroproteins,] proteoglycans, glycoproteins, neural adhesion molecules, [cell signalling molecules and mixtures, thereof] and mixtures thereof.

Claim 52 (Amended):

The method according to claim 50, wherein said differentiation agent is a mixture of retinoic acid and NGF.

Claim 53 (Amended):

The method according to [claim 50] claim 51, wherein said neuronal cells are selected from the group consisting of mesencephalic cells and striatal cells.

Claim 54 (Amended):

A method of producing a pharmaceutical composition comprising neural cells obtained from umbilical cord blood comprising:

[a.] (a) obtaining a sample of mononuclear cells from said umbilical cord blood, wherein said mononuclear cells comprise stem or progenitor cells;

[b.] (b) selecting for and isolating [a sample of] said pluripotent stem or progenitor cells within said sample of mononuclear cells;

[c.] (c) growing said stem or progenitor cells from step(b) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said stem or progenitor cells to neural.; and

[d.] (d) combining said [cell obtained from step b] cells obtained from step (c) with a pharmaceutically acceptable carrier, additive or excipient.

Claim 55 (Amended):

The method according to claim 54, wherein said selecting and isolating step (b) is carried out using a magnetic cell separator to separate out cells containing a CD marker.

Claim 56 (Amended):

The method according to claim 54, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine, erthyopoietin, thrombopoietin, silencers, SHC, [neuroproteins,] proteoglycans, glycoproteins, neural adhesion molecules, [cell signalling molecules and mixtures, thereof] and mixtures thereof.

Claim 57 (Amended):

A method of producing a pharmaceutical composition comprising neural cells obtained from umbilical cord blood comprising:

[a.] (a) obtaining a sample of mononuclear cells from said umbilical cord blood, wherein said mononuclear cells comprise pluripotent stem or progenitor cells;

[b.] (b) growing said mononuclear cells from step [b] (a) in a culture medium containing an effective amount of a differentiation agent for a period sufficient to change the phenotype of said pluripotent stem or progenitor cells within said sample of mononuclear cells to neural; and

[c.] (c) selecting for and isolating said [neural cells] cells having a neural phenotype from said [sample of] pluripotent stem or progenitor cells within said sample of mononuclear cells by essentially eliminating from said sample mononuclear cells having a CD marker; and

[d.] (d) combining said [neural cells] cells having a neural phenotype isolated from step (c) with a pharmaceutically acceptable carrier, additive or excipient.

Claim 58 (Amended):

The method according to claim 57, wherein said selecting and isolating step (c) is carried out using a magnetic cell separator to separate out cells containing a CD marker.

Claim 59 (Amended):

The method according to claim 57, wherein said differentiation agent is selected from the group consisting of retinoic acid, fetal or mature neuronal cells, BDNF, GDNF, NGF, FGF, TGF, CNTF, BMP, LIF, GGF, TNF, IGF, CSF, KIT, interferon, triiodothyronine, thyroxine,

erythropoietin, thrombopoietin, silencers, SHC, [neuroproteins,] proteoglycans, glycoproteins, neural adhesion molecules, [cell signalling molecules and mixtures, thereof] and mixtures thereof.

Claim 60 (Amended):

The method according to claim 57, wherein said differentiation agent is a mixture of retinoic acid and nerve growth factor.

Claim 61 (Amended):

The method according to claim 57, wherein said [neuronal cells] cells having a neural phenotype are selected from the group consisting of mesencephalic cells and striatal cells.